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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of
BRANSTROM et al.



TECH CENTER 1600/2300

Appln. No. 08/711,961

Group Art Unit: 1636

Filed: September 6, 1996

Examiner: I. Yucel

Title: BACTERIAL DELIVERY SYSTEM

* * * * *

November 29, 2000

APPEAL BRIEF

Hon. Commissioner of Patents
and Trademarks
Washington, D C. 20231

Sir:

Appellants submit herewith their Appeal brief in
triplicate, pursuant to 37 C.F.R. §1.192.

REAL PARTY IN INTEREST

The real party in interest is the Government of the
United States of America, as represented by the Secretary,
Department of Defense, by virtue of assignment from the
Applicants.

RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to the
Appellants or the Appellants' legal representative, or the
assignee, that will directly affect or will be directly
affected by or have bearing on the Board's decision in this
appeal..

See Answer due 2 months

STATUS OF CLAIMS:

Claims 45-55 have been finally rejected by the Examiner and are at issue in this appeal. The claims on appeal are set forth in the Appendix to this brief.

STATUS OF AMENDMENTS:

One response has been submitted subsequent to the Examiner's final rejection of March 3, 2000. No amendments were filed after the final rejection.

SUMMARY OF THE INVENTION:

The invention is a method for introducing functional DNA into animal cells using a bacterial delivery system. A bacterial vector capable of delivering functional DNA to cells is produced by introducing a bacterial plasmid containing functional DNA into mutated bacteria, the mutated bacteria having an attenuating factor which will result in lysis of the bacteria after entry into a cell (described, for example, at page 4, lines 11-23, and page 7, lines 3-7 of the specification). The bacteria are administered to a cell, enter the cell, and lyse, thereby delivering to the cell the DNA capable of being expressed therein. In a particularly preferred embodiment, a mutated strain of *Shigella* that is unable to synthesize active aspartate β -semialdehyde dehydrogenase of the DAP pathway delivers DNA to a mucosal epithelium cell (described, for example, at page 5, lines 1-11

of the specification). Dependent claims recite preferred target cells and bacterial species and strains.

ISSUE:

Whether the Examiner's rejection of claims 45-55 under 35 U.S.C. § 102(e), as being unpatentable over Powell et al. (U.S. Patent 5,877,159) should be reversed.

It is noted that claims 45-55 also stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent 5,824,538. Appellants have indicated their willingness to file a terminal disclaimer at the time that the claims are indicated to be otherwise allowable.

GROUPING OF THE CLAIMS:

While the Examiner has grouped claims 45-55 together in the §102(e) rejection, the Appellants believe, for the reasons discussed below, that features of claim 53 and the dependent claims (claims 46-52 and 54-55) need to be considered separately in deciding the patentability issue.

THE EXAMINER'S POSITION:

The Examiner rejected claims 45-55 under 35 USC § 102(e) as being anticipated by Powell et al. (U.S. Pat. No. 5,877,159). The Examiner stated in the Office Action of July 19, 2000, that

"Powell et al. broadly disclose and claim delivery of 'live invasive bacteria' which comprise a 'eukaryotic expression cassette encoding genes.' The purpose of the 'eukaryotic expression cassette' is that the animal infected by the invasive bacteria will express the cassette and produce an antigen which acts as a vaccine." (paper no. 19, page 3, lines 13-16)

It is the Examiner's position that "[t]his is exactly the same concept used by applicant in the instant application." (paper no. 19, page 3, lines 16-17).

ARGUMENT:

Appellants respectfully submit that the Examiner's reasoning is an insufficient basis for a rejection under 35 USC § 102(e), and that the claims under appeal are not anticipated by Powell et al.

The Powell et al. patent discloses and claims

"a method for introducing and expressing a gene in animal cells comprising infecting said animal cells with live invasive bacteria, wherein said bacteria contain a eukaryotic expression cassette encoding said gene, wherein said gene encodes a vaccine antigen, wherein said vaccine antigen is expressed at detectable levels, and wherein said animals cells are cultured in vitro." (see Claim 1 of the patent).

In contrast, the present application claims a method for the delivery of exogenous DNA capable of being expressed in an animal cell, which includes introducing said DNA into mutated bacteria, administering said bacteria to said cell, such that the bacteria, once inside the cell, will lyse, thereby delivering to the cell the DNA capable of being expressed therein. (See, for example, claim 45). Appellants submit that the invention disclosed and claimed in Powell et al. does not

contain each and every element of the presently claimed invention, as is required for a 35 USC §102(e) rejection. It is particularly noted that the claims of Powell et al. are limited to methods involving a gene that encodes a vaccine antigen, expressed at detectable or effective levels, a limitation that is not present in any of pending claims 45-55. Each of the claims on appeal explicitly or implicitly include the step of introducing said DNA into mutated bacteria, a step that is not found in any of the claims of Powell et al. Appellants' claim 53 more specifically recites the step of introducing said DNA into a mutated strain of *Shigella* which is unable to synthesize active aspartate β -semialdehyde dehydrogenase of the DAP pathway, a step which is not found in any of the Powell et al. claims. Furthermore, none of the Powell claims indicates that exogenous DNA is introduced to intestinal mucosal epithelium, as recited in dependent claim 51. Appellants submit that the Examiner has failed to indicate which claim or claims of the '159 patent are considered to claim the same invention as pending claims 45-55 of the present application.

It is therefore respectfully submitted that the Powell et al. patent does not, in fact, claim the same invention as the presently pending application, although certain aspects of the invention may be disclosed in the specification thereof.

With regard to any aspects of the presently claimed invention that may have been suggested or disclosed in the

specification of the Powell et al. patent, Appellants respectfully direct the Board's attention to the Rule 131 Declaration of Dr. Donata Sizemore, filed on January 19, 2000 with paper no. 20. The Declaration provides evidence demonstrating that the presently claimed invention was made prior to May 3, 1995, the priority date of U.S.-Pat. No. 5,877,159. The Examiner indicated that the Declaration was insufficient to overcome the Powell et al. patent because Powell et al. allegedly claims the same invention. As discussed hereinabove, Appellants disagree that the Powell et al. patent claims the same invention as Appellants'. The Examiner has not provided an indication as to which claims are considered to correspond to Appellants' invention, nor shown that each and every element of Appellants' invention is recited in such claims.

The Declaration filed on January 19, 2000, clearly establishes that the present invention was made prior to the priority date of the '159 patent. Consideration of the Declaration and reversal of the rejection are respectfully requested.

CONCLUSION:

In summary, Appellants submit that

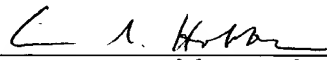
- 1) None of the claims of Powell et al. contains each and every element of claims 45-55, on appeal in the present case; and

BRANSTROM et al. -- Appln. No. 08/711,961

2) The Declaration of Dr. Donata Sizemore under Rule 131 establishes that the present invention was made prior to the priority date of the Powell et al. application. For these reasons, it is respectfully requested that the 35 USC § 102(e) rejection be reversed.

Respectfully submitted,

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Appendix

45. A method for the delivery of exogenous DNA capable of being expressed in an animal cell, said method comprising:

- (i) introducing said DNA into mutated bacteria, said bacteria having an attenuating factor which will result in lysis of the bacteria after entry into said cell; and
- (ii) administering said bacteria to said cell, such that the bacteria, once inside the cell, will lyse, thereby delivering to the cell the DNA capable of being expressed therein.

46. The method of claim 45 wherein said animal cell is a mammalian cell.

47. The method of claim 45 wherein said bacteria is *Shigella*.

48. The method of claim 47 wherein said *Shigella* is *S. flexneri*.

49. The method of claim 48 wherein said *S. flexneri* is 15D.

50. The method of claim 47 wherein said cell is a cell of mucosal epithelium.

51. The method of claim 50 wherein said epithelium is intestinal mucosal epithelium.

52. The method of claim 47 wherein said *Shigella* is further inactivated.

53. A method for delivering DNA capable of being expressed in a mucosal epithelium cell, said method

comprising:

- (i) introducing said DNA into a mutated strain of *Shigella* which is unable to synthesize active aspartate β -semialdehyde dehydrogenase of the DAP pathway; and
- (ii) administering the *Shigella* of (i) to a mucosal epithelium cell such that the *Shigella*, after uptake by said cell, will lyse, thereby delivering to the cell the DNA capable of being expressed therein.

54. The method of claim 53, wherein said mucosal epithelium is an intestinal mucosal epithelium cell.

55. The method of claim 53, wherein said *Shigella* is further inactivated.